REMARKS

The Amendments

The kit claims have been canceled. The claims have further been clarified to exclude all iodine radionuclides. Also, the dependency of claims 8 and 21 has been modified and claim 21 further amended to provide proper antecedent basis. Finally, the "small organic compound" embodiments have been removed in light of the 35 U.S.C. §112 rejection.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Restriction Requirement

Although applicants remain of the opinion that the restriction is improper, the kit claims have been cancelled to expedite prosecution of the composition claims. The kit claims will be reserved for filing in a divisional application, if desired. Thus, the restriction requirement is rendered moot. The "withdrawn" claims that remain pending are withdrawn pursuant to the election of species, not the restriction requirement.

The Rejection under 35 U.S.C. §112, paragraph

The rejection under 35 U.S.C. §112, second paragraph, is rendered moot by the above

amendments.

The Rejections under 35 U.S.C. §102

The 35 U.S.C. §102 anticipation rejections of claims 1, 4, 6, 11, 14 and 16 over Russell (US Pub 2003/0235532) and of claims 1, 4, 6, 14 and 16 over Thakur (U.S. Patent No. 6,395,255) are respectfully traversed.

It is believed that these rejections are overcome by the above amendments clarifying the exclusion as to the radionuclide. From the disclosure as a whole, it is evident that the iodide ion stabilizer used according to the invention is a separate component from the radionuclide. Thus, the iodide ion is not provided from an iodine radionuclide. The claims are amended above to reflect the clarification inherent in the disclosure.

The references fail to disclose a composition or method which has:

- a radionuclide, excluding iodine radionuclides and
- iodide ions or a compound which releases or generates iodide ions.

The Office Action points to the iodine isotope as the source of iodide ions. The reference compositions/methods, thus, either contain a radionuclide which is not iodine but no iodide ions or contain an iodine radionuclide, which allegedly provides the iodide ions. But, the references do not meet both above-recited claim elements. Thus, the references do not anticipate any of the instant claims.

Further, the references would not support a 35 U.S.C. §103 rejection. There is no motivation to add iodide ions to the reference compositions when a non-iodine radionuclide is used.

Accordingly, the rejections over these references should be withdrawn.

The Rejections under 35 U.S.C. §103

The rejections of claims 1-4, 6, 10-14, 16, 18-20 and 32-34 under 35 U.S.C. §103, as being obvious over Miller (U.S. Patent No. 6,174,513) in view of Bannerjee (US Pub 2002/0151598), or further in view of Blum are respectfully traversed.

Initially, it is pointed out that Bannerjee is not necessarily prior art to the instant application. The Bannerjee publication is of an application filed May 3, 2002, which is a divisional of an application filed June 22, 2001. The filing dates of both of these applications are after applicants' filing date of May 16, 2001. The publication also indicates priority to a provisional application filed April 17, 2001. Although this provisional filing date is before applicants' filing date, the record does not indicate what the provisional application discloses. The Bannerjee publication is only prior to applicants' filing date for what has an enabling disclosure in the provisional application. To support the rejection, the PTO must provide the provisional disclosure to establish the proper applicability of Bannerjee. The burden rests with the PTO to support the rejection and, currently, it is unsupported on the record. The only showing on the record, with regards to Bannerjee, is a disclosure after applicants' filing date. If the proper support cannot be provided, the rejection should be withdrawn at least on this basis.

Assuming without admission that the Bannerjee provisional supports all the disclosure of the publication, Applicants also maintain their previous arguments that there is not proper motivation to combine the references and, even if combined, the combination would not suggest the claimed invention. These arguments are re-phrased and supplemented below.

Miller teaches compositions and methods for stabilizing radiolabeled peptides and proteins contained in a diagnostic or therapeutic radiopharmaceutical composition by use of surfactants alone or surfactants in combination with salts. Miller teaches that the

radiolabeled peptides or proteins contain a radionuclide and a carrier agent designed to target a specific organ or tissue site in the body, with the radionuclide optionally being affixed to the carrier. See, e.g., col. 1, lines 15-23 and 46-54. The optional salts disclosed for use by Miller are the chloride salts listed at col. 5, lines 42-43.

As established, Miller lacks any teaching or suggestion of including in its compositions a compound which provides or generates iodide ions.

Bannerjee teaches compositions and methods for treating symptoms of bronchoconstrictive disorders, such as asthma. The compositions contain a bronchodilating agent, such as described in paragraphs [0008] - [0010] of the publication. The compositions are provided in a stabilized solution form which gives them long shelf life, i.e., in terms of 1-3 years. See, e.g., paragraph [0006]. Bannerjee teaches as an optional embodiment of its invention that tonicity adjusting agents may be added to its compositions, paragraph [0056]. The about 70 particular examples of various types of such agents include potassium iodide and sodium iodide. These are the only two iodide agents mentioned. Bannerjee teaches nothing at all regarding stabilizing radiolabeled peptides or proteins or anything even remotely related thereto.

The apparent basis for the rejection is that it would have been obvious to one of ordinary skill in the art, in view of Bannerjee, to do all of the following:

- adjust the tonicity of the radiolabeled peptides or protein compositions of Miller,
- select the method of Bannerjee, relating to compositions for treating bronchoconstrictive disorders, as a method for adjusting tonicity of the radiolabeled peptides or protein compositions of Miller,
- select from the Bannerjee method potassium iodide or sodium iodide as the tonicity adjusting agent from the 70 listed by Bannerjee; and

- recognize or find inherent that, by making such a modification to Miller, the iodide ions would stabilize the radionuclides in the Miller compositions.

Applicants respectfully disagree that the prior art supports such conclusions.

In order to establish obviousness under 35 U.S.C. § 103, the mere fact that the prior art could be modified or two prior art references combined to arrive at the claimed invention is insufficient. The prior art must suggest to one of ordinary skill in the art the desirability of the necessary modification or combination. See In re Laskowski, 10 USPQ2d 1397 (Fed. Cir. 1989); and, In re Geiger, 2 USPQ2d 1276 (Fed. Cir. 1987). There is no desirability provided by the references, i.e., no motivation, for one of ordinary skill in the art to adjust the tonicity of the Miller compositions by applying the method of Bannerjee. The only suggestion for such combination comes from the desire to support the rejection by picking out disclosures of the references to meet applicants' claims. But use of applicants' own teachings to provide the motivation for combining references is not proper under 35 U.S.C. §103.

There is no suggestion from Miller that there is any need or desire to adjust the tonicity of the Miller compositions. There is also no teaching in Miller which would give one of ordinary skill in the art a reasonable expectation that a tonicity adjusting agent could be successfully used in their compositions or that it would not, in fact, be harmful to the Miller compositions. Further, there is no suggestion from Bannerjee or from Miller to suggest that a means for adjusting tonicity in a composition for effecting bronchodilating activity would be desired or even useful in a composition, such as Miller's, containing a radiopharmaceutical. The compositions of Bannerjee and Miller are completely unrelated in terms of constituents, activities and applications. One of ordinary skill in the art would not have a reasonable expectation that a tonicity adjusting teaching for one type of composition would work – and

would not be detrimental – in a completely different composition. In order to establish obviousness under 35 U.S.C. §103, the prior art must contain both a suggestion of the claimed method and provide a reasonable expectation of success for such method. See In re Vaeck, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); and In re Dow Chemical Co., 5 USPQ2d 1529 (Fed. Cir. 1988). Here there is neither.

The previous Advisory Action alleged that, merely because the Miller, Blum and Bannerjee references are all directed to pharmaceutical compositions administered in vivo in saline solution, it would be obvious to combine teachings of one reference with another. Applicants respectfully disagree that one of ordinary skill in the art would be motivated to modify one pharmaceutical composition by adding elements of any other pharmaceutical composition merely because they are both saline solution pharmaceuticals. Under such a test, no combination of two known pharmaceutical ingredients could ever be patentable. This cannot be the proper test. As stated in Intra Corp. v. Hamar Laser, 4 USPQ2d 1337, 1352 (E.D.Mich. 1987), *aff'd*, 862 F.2d 320 (Fed. Cir. 1988)(unpublished): "Most patentable inventions combine old elements .. [and such] fact .. is irrelevant to the legal determination of obviousness under § 103..". See also In re Rouffet, 149 F.3d 1350, 47 USPQ 2d 1453 (Fed. Cir. 1998), and the previously cited In re Laskowski; and In re Geiger. In the current Office Action, it is alleged that applicants misconstrued the point made in the Advisory Action. Applicants do not believe they misconstrued the argument. That both references relate to pharmaceuticals which are administered in vivo and in saline solution does not make them much more similar than other pharmaceuticals. All pharmaceuticals are administered in vivo and a large variety are administered in saline solution. Applicants remain of the position that it would not be obvious to combine any two ingredients from two different pharmaceutical compositions merely because those compositions are both pharmaceuticals for in vivo administration in saline solution.

There is no desirability indicated in the references, i.e., no motivation, for why one of ordinary skill in the art would want to adjust the tonicity of the Miller compositions by applying the method of Bannerjee. First, there is no teaching in Miller to suggest that there is any need or desire to adjust the tonicity of their compositions. There is also no teaching in Miller which would lead one of ordinary skill in the art to believe: 1) that a tonicity adjusting agent would not, in fact, be harmful to the objectives of the Miller invention or 2) that a tonicity adjusting agent for bronchodilating compositions would be useful for a radiopharmaceutical composition. The compositions of Bannerjee are completely unrelated to those of Miller in terms of constituents, activities and applications and thus there is no reasonable expectation that the tonicity adjusting agent of Bannerjee would work in the completely different radiopharmaceutical compositions.

Applicants do not understand the statement in the Office Action that the "rejection does not apply the method of Bannerjee." If the tonicity adjusting method of Bannerjee is not applied, there is no teaching at all regarding use of an iodide. In order to apply the teaching in Bannerjee regarding use of an iodide, the reference must be considered as a whole. It is impermissible to take a single teaching from a reference without considering all the teachings of the reference. Thus, the fact that Bannerjee relates to adjusting tonicity of bronchodilating compositions, i.e., compositions having no relation to radiopharmaceuticals, must be considered. The non-analogous nature of Bannerjee and Miller is such that one of ordinary skill in the art would not have even considered Bannerjee to provide teachings for modifying the Miller compositions. The references are not in the same field of endeavor nor reasonably pertinent to a particular problem with which the other reference is involved. See, In re Deminski, 230 USPQ 313 (Fed. Cir. 1986); and, In re Clay, 23 USPQ2d 1058, 1061 (Fed. Cir. 1992).

The Office Action further alleges that tonicity is a concern for all pharmaceutical compositions. That may or may not be true; there is no evidence on the record to support this allegation though. To the contrary, Bannerjee teaches that tonicity agents are merely optional and "may" be added. Thus, it is clear that they are not required or desired in all pharmaceutical saline compositions. Certainly, Miller discusses no need for adjusting tonicity of its compositions. Even if it were true, it does not mean that a method for adjusting tonicity for one type of composition would be reasonably be expected to be successful for adjusting tonicity of a completely different kind of composition. Nor is there any suggestion that the particular embodiment of Bannerjee using an iodide compound would be reasonably expected to be successful for adjusting tonicity of radiopharmaceutical compositions. The Office Action alleges that all the Bannerjee tonicity adjusting agents are equivalent. But Bannerjee does not teach this. To the contrary, Bannerjee implies that the agents are of differing strengths because they are use to "provide the desired ionic strength." Again, there is no suggestion whether tonicity agents are necessary or desired for Miller's radiopharmaceutical compositions or that the iodide agents would be useful in connection with Miller's radiopharmaceutical compositions.

It is alleged in the Office Action that the stabilization of the radiopharmaceutical would result from the characteristic properties of the suggested combined compositions. But the advantage in radionuclide stabilization would only be achieved on 2 out of 70 chance the iodide salt is selected from all the agents of Bannerjee. Thus, it is not an inherent property of the Bannerjee tonicity agents because stabilizing a radiopharmaceutical would not "necessarily and inevitably" occur. It only would occur when the iodides are selected and there is no suggestion to make that particular selection.

As a further basis for nonobviousness, the references fail to teach or suggest use of an iodide agent in an amount sufficient to "stabilize the composition against degradation thus

maintaining high radiochemical purity of the composition." The Office Action alleges that this argument is not persuasive because the claims do not recite any amounts. This is not correct. The claims literally recite the above-quoted language. Although a numerical amount is not recited, there is a functional amount recitation in the claims and there is no suggestion that the small amounts which would be used for tonicity adjustment would provide such a function. That the references teach nothing about the stabilizing effect of iodide in a radiopharmaceutical, shows that there is no proof on the record that the amount necessary for such result is taught.

Blum, like Miller, teaches nothing about combining iodide ions with a radiopharmaceutical. For reasons analogous to those discussed above, it would not have been obvious to one of ordinary skill in the art to modify the depreotide compositions of Blum to provide iodide ions for stabilizing the radiopharmaceutical. Even if Miller were modified to use the depreotide agent of Blum, there would be no suggestion to apply the teaching of Bannerjee to such a composition, nor any other teachings suggesting applicants' invention.

For all of the above reasons, it is again urged that the rejections under 35 U.S.C. § 103 should be withdrawn. One of ordinary skill in the art would not have been motivated to combine the Miller and Bannerjee references in the manner suggested in the Office Action and, even if such combination were made, all elements of the instant claims are not fairly suggested.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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